## REMARKS

Claims 26-48 are pending in this application. Claims 26-28 and 40-46 are under examination and claims 29-39, 47 and 48 have been withdrawn from consideration because they are directed to a non-elected invention or species. Claim 26 has been amended. The amendments to claim 26 are fully supported by the specification and do not introduce new matter. After entry of the present Amendment, claims 26-48 will be pending in the present application.

### Information Disclosure Statement

Applicant notes that references C09, C10, C11, C12, C37, C38, C39 and C40 were crossed out on the PTO-1449 Forms filed July 20, 2007 for failure to provide a date.

Applicant is submitting herewith a Supplemental Information Disclosure Statement with a revised PTO-1449 that includes the dates for the references previously cited as C09, C10, C11, C12, C37, C38, C39 and C40 (resubmitted as references C82, C83, C84, C85, C99, C100, C101 and C102). Applicant respectfully requests that the Examiner consider these references and the other references listed on the revised PTO 1449 Form submitted herewith.

### The Rejection under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 26-28, 40-42 and 45-46 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Greer, 1986, Molecular and Cellular Biology, 6:635-644 ("Greer"), in combination with Rana, International Publication No. WO 01/25486 A1 ("Rana") and Li *et al.*, 1998, Science, 280:279-284 ("Li"). Claims 42, 43 and 44 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Greer, in combination with Rana and Li, and in further view of Kaminska *et al.*, 2002, FEMS Yeast Research, 2: 31-37 ("Kaminska"). For the reasons below, the rejections should be withdrawn.

A finding of obviousness requires that "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. §103(a). In its recent decision addressing the issue of obviousness, *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 82 USPQ2d 1385 (2007), the Supreme Court stated that the following factors set forth in *Graham v. John*

*Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966) still control an obviousness inquiry: (1) the scope and content of the prior art; (2) the differences between the prior art and the claimed invention; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness. *KSR*, 127 S.Ct. at 1734, 82 USPQ2d at 1388 quoting *Graham*, 383 U.S. at 17-18, 14 USPQ at 467.

The *KSR* Court rejected a rigid application of the "teaching, suggestion, or motivation" test previously applied by the Court of Appeals for the Federal Circuit. *KSR*, 127 S. Ct. at 1739 USPQ2d at 1395. However, the Supreme Court affirmed that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does . . . because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *KSR*, S.Ct. at 1741, 82 USPQ2d at 1396. Thus, consistent with the principles enunciated in *KSR*, a *prima facie* case of obviousness can only be established by showing a suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference and to carry out the modification with a reasonable expectation of success, viewed in light of the prior art.

Thus, the principles set forth in *Graham*—which are still good law post-KSR—require that both the suggestion and the expectation of success must be found in the prior art, and not derived from knowledge gained from the applicant's disclosure.

After the *KSR* decision, the Board of Patent Appeals and Interferences has continued to shape the contours of the obviousness inquiry. The Supreme Court in *KSR* stated that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 127 S.Ct. at 1741, 82 USPQ2d at 1389. Following *KSR*, the Board stated that "[i]t is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art." *Ex Parte El-Naggar*, WL 2814131 at *3 (BPAI 2007) (citing *In re Hedges*, 783 F.2d 1038, 1041 (Fed. Cir. 1986) (quoting *In re Wesslau*, 353 F.2d 238, 241 (C.C.P.A. 1965))).

The focus of Greer is to understand the excision and ligation steps involved in the splicing of precursor tRNA in yeast, specifically *S. cerevisiae*. Greer describes methods for measuring the activity of yeast and T4 tRNA ligases by incubating pre-tRNA halves with

tRNA ligase and [γ-32]-ATP and measuring the incorporation of label from the labeled ATP into the tRNA product (*see* Greer p. 637, Col. 1, lines 8-46). Further, in an attempt to determine whether the excision and ligation steps of the splicing pathway are independent rather than concerted, Greer describes a competition assay between yeast tRNA ligase and T4 RNA ligase, whereby the differences between the ligation products of yeast ligase and T4 ligase are used to distinguish between a concerted and an independent method of ligation (*see* Greer, p. 635, Col. 2, line 20 to p. 636, Col. 2, line 14).

Greer does not teach or suggest screening assays to identify compounds that modulate the activity of yeast tRNA ligase, much less screening assays to identify compounds that modulate the activity of animalia tRNA ligase. In fact, there is no teaching or suggestion to use animalia tRNA ligase at all in Greer. Moreover, Greer does not provide any motivation to one of ordinary skill in the art to screen for compounds that modulate the activity of animalia tRNA ligase.

Rana does not cure the deficiencies of Greer. Rana relates to methods for identifying compounds that bind to a target RNA molecule (*see* Rana, abstract). In particular, Rana describes methods for identifying compounds that bind to a target RNA molecule by " (a) contacting a dye-labeled target RNA molecule with substantially one type of test compound attached to a solid support, thereby providing a dye-labeled target RNA: support-attached test compound complex; and (b) determining the structure of the substantially one type of test compound of the RNA: test compound complex" (*see* Rana, p. 3, lines 28-33). Rana indicates that some compounds that are identified as binding to *mRNA* (not tRNA) may be useful in increasing or decreasing protein production and thus, may be useful in treating diseases (*see* Rana, abstract; *see* also p. 8, lines 11-25).

Rana does not teach or suggest screening for compounds that modulate the activity of an enzyme, much less an animalia tRNA ligase. The focus of Rana is assays to identify compounds that *bind* to a target RNA molecule. In fact, Rana does not even mention tRNA splicing ligase, much less provide any assays for evaluating whether a compound can modulate the activity of a tRNA splicing ligase. Moreover, the description in Rana relating to modulating protein production and treating or preventing diseases relates to *mRNA*, not precursor tRNA or pre-tRNA half-molecules, which are substrates for eukaryotic tRNA splicing ligase. Thus, contrary to the Examiner's allegation, one of ordinary skill in the art would not have been motivated to modify the methods of Rana for identifying compounds that bind to a target RNA molecule to develop a method for identifying compounds that modulate the activity of an animalia tRNA splicing ligase, even in view of Greer which

relates to understanding the splicing of tRNA precursors in *S. cerevisiae*.

Li does not cure the deficiencies of Greer and Rana, taken either alone or in combination. Li relates to the crystal structure of the endonuclease of *Methanococcus jannaschii*, an archaeon. Li describes the general mechanism for removal of tRNA introns in eucarya. However, the focus of Li is archaeon endonucleases, not archaeon, yeast or animalia ligases. Moreover, there is no teaching or suggestion in Li that yeast tRNA splicing ligase can be substituted with the animalia tRNA ligase.

Kaminska does not cure the deficiencies of Greer, Rana and Li, taken either alone or in combination. Kaminska relates to the interaction between the yeast tRNA isopentenylation pathway and the yeast isoprenoid biosynthetic pathway (IBP). Kaminska teaches that both the isoprenoid pathway and the tRNA isopentenylation pathway compete for the same substrate, DMAPP; as a result, "tRNA levels appear to contribute to the regulation of the isoprenoid pathway" (*see* Kaminska, p. 32, Col. 1, lines 13-15 and lines 29-31). Kaminska suggests that levels of an enzyme in the isoprenoid pathway may regulate tRNA modification and that tRNA levels may contribute to the regulation of the isoprenoid pathway (Kaminska, abstract and p. 32, Col. 1, lines 17-19 and 29-31).

Kaminska does not teach or suggest tRNA splicing. There is no teaching or suggestion in Kaminska regarding tRNA splicing ligase or the use of such a ligase in a method for screening for compounds that modulate tRNA splicing ligase, much less an animalia tRNA splicing ligase or the use of an animalia tRNA splicing ligase in such a screening method. Moreover, there is no teaching or suggestion in Kaminska that an isoprenoid compound would have any affect on tRNA splicing, much less an animalia tRNA splicing ligase.

Based on the teachings of Kaminska, taken alone or in combination with Greer and Li, it is unclear how the relationship between tRNA levels and tRNA isopentenylation and the isoprenoid pathway would suggest that using an isoprenoid compound would have any effect on the activity of an animalia tRNA splicing ligase. In particular, it is unclear how the teaching in Kaminska of the competition between tRNA isopentenyltransferase and an enzyme in the isoprenoid biosynthetic pathway for the substrate DMAPP would have suggested screening for an isoprenoid compound that modulated tRNA splicing. Accordingly, Kaminska would not have provided one of ordinary skill in the art with a motivation to screen for an isoprenoid compound that modulates the activity of an animalia tRNA splicing ligase.

Thus, Greer, Rana, Li and Kaminska, taken alone or in any combination, do not

render claims 26-28 and 40-46 obvious. In view of the foregoing, the rejections of claims 26-28 and 40-46 under 35 U.S.C. 103(a) should be withdrawn.

## CONCLUSION

Applicant believes that the present claims meet all of the requirements for patentability. Consideration and entry of the amendments and remarks made herein into the file history of the present application are respectfully requested. The Examiner is invited to contact the undersigned if any issues remain.

Respectfully submitted,

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